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P/42-60

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Patent Application of

Fabrizio SAMARITANI et al.

Serial No.: 08/737,633

Filed: November 15, 1996

For: IFN-BETA LIQUID FORMULATIONS

Date: October 19, 2000

Group Art Unit: 1646

Examiner: D. Fitzgerald

Assistant Commissioner for Patents
Washington, D.C. 20231

APPEAL BRIEF TRANSMITTAL LETTER - FEE COMPUTATION

Sir:

Transmitted herewith in triplicate is an Appeal Brief in the above-identified application.

OFGS Check No. 1734, which includes the fee of $310.00, is enclosed.

In the event the actual fee is greater than the payment submitted or is inadvertently not enclosed or if any additional fee during the prosecution of this application is not paid, the Patent Office is authorized to charge the underpayment to Deposit Account No. 15-0700.

If this communication is filed after the shortened statutory time period had elapsed and no separate Petition is enclosed, the Commissioner of Patents and Trademarks is petitioned, under 37 C.F.R. §1.136(a), to extend the time for filing a response to the outstanding Office Action by the number of months which will avoid abandonment under 37 C.F.R. §1.135. The fee under 37 C.F.R. § 1.17 should be charged to our Deposit Account No. 15-0700.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed: Assistant Commissioner for Patents, Washington, D.C. 20231, on October 19, 2000:

Charles C. Achkar
Name of applicant, assignee or Registered Representative

Charles Achkar
Signature

October 19, 2000
Date of Signature

EAM/CCA:lac

Respectfully submitted,

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M.J.
10/20/00

Assistant Commissioner for Patents
Washington, D.C. 20231

APPEAL BRIEF UNDER 37 C.F.R. §1.192

Sir:

This appeal concerns the propriety of the Examiner's final rejection of pending claims 1, 3, 5-7, 9 and 10 in this application. A fee of $310.00 as set forth in 37 CFR §1.17(c) is enclosed herewith.

Real Party in Interest

The assignee of this application is Applied Research Systems ARS Holding N.V.

Related Appeals and Interferences

There are no known related appeals or interference proceedings.

Status of Claims

The claims pending in this application are numbers 1 and 3-10 with claims 1, 3, 5-7, 9 and 10 the subject of this appeal. Claims 4 and 8 were objected to as being dependent on a rejected claim. All other claims which at any time were pending in this case have been canceled.

Status of Amendments

The December 17, 1999 Amendment has been entered.

Summary of Invention

Disclosed in this application is a liquid pharmaceutical formulation consisting of from about 0.6 to 24 MIU/ml of interferon-beta, mannitol, a buffer capable at a pH of the between 3.0 and 4.0 and, optionally, albumin.

Issues

Claims 1, 3, 7, 9 and 10 are rejected under 35 U.S.C. §103 over Hanisch '566. Claim 5 is rejected under 35 U.S.C. §103 over Hanisch '566 in view of Cymbalista '454. Claim 6 is rejected over Hanisch '566 in view of Hershenson '605.

The Examiner alleges that it would be obvious to formulate a liquid β-IFN composition consisting of from about 0.6 to 24 MIU/ml of interferon-beta and containing mannitol as the sole polyol because Hanisch teaches compositions containing interferon-beta, albumin, a buffer with or without a stabilizer. However, the Examiner acknowledged that Hanisch does not exemplify a formulation consisting of interferon-beta, albumin, a buffer and mannitol.

The Examiner also alleges that Cymbalista teaches that acetate buffer at a pH of 3.5 is suitable for making stable formulations of interferon-beta. The Examiner further alleges that Hershenson teaches that it is desirable to employ a buffer at a pH between 2 and 4 to prepare stable formulations of interferon-beta.

Grouping of Claims

Rejected claims 1, 3, 5-7, 9 and 10 stand or fall together.

Argument

Claim 1 in this application sets forth a **liquid** pharmaceutical formulation consisting of from about 0.6 to 24 MIU/ml of interferon-beta, **mannitol**, a buffer at a **pH between 3.0 and 4.0** and, optionally, albumin. This is neither taught nor suggested by the references whether considered alone or in combination.

In contrast, Hanisch relates to pharmaceutical compositions comprising interferon-beta, a stabilizer and human serum albumin which composition is then **lyophilized**. Accordingly, the Hanisch compositions differ from the composition of the present invention in several aspects. First, the compositions of Hanisch contain dextrose while the presently claimed compositions contain mannitol. Second, the compositions of Hanisch as acknowledged by the Examiner contain higher concentrations of interferon-beta (50 MIU/ml) immediately prior to lyophilization which implies that these higher concentrations are necessary to achieve stability and to efficiency

during lyophilization. Accordingly, there is nothing in Hanisch either alone or in combination with the other cited references (i.e., Cymbalista and Hershenson) that teaches or suggests the composition of the present invention which is a liquid pharmaceutical composition containing interferon-beta and mannitol.

In addition to the obvious difference in that the claimed composition of a low concentration of interferon-beta is stable in the liquid state, Hanisch also differs in that it teaches that human plasma protein factor (PPF) is the preferred stabilizer for low pH formulations (see column 9, lines 43-44). Furthermore, Hanisch also teaches that a mixture of human serum albumin (HSA) and dextrose or HSA alone is preferably used at high pH (column 9, lines 40-42), in contrast to the optional use of albumin in the present invention at low pH. Applicants maintain that there is nothing in Hanisch either alone or in combination with Cymbalista and Hershenson that teaches the use of mannitol (a carbohydrate) at low pH in a stable liquid composition containing interferon-beta. On the contrary, Hanisch teaches the use of a protein (PPF) at low pH and a carbohydrate (dextrose) at high pH. Therefore, a person skilled in the art would not have any expectation of success using mannitol, a carbohydrate, to stabilize low concentrations of interferon-beta in a liquid state (not lyophilized) at a low pH.

Conclusion

As demonstrated above, none of the references teach or suggest alone or in combination.

Reversal of the final rejection and allowance of this application is, therefore, respectfully solicited.

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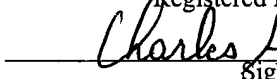
Name of applicant, assignee or Registered Representative



Signature

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APPENDIX

The Claims on Appeal Are:

1. A liquid pharmaceutical formulation consisting of from about 0.6 to 24 MIU/ml of interferon-beta, mannitol, a buffer at a pH between 3.0 and 4.0 and, optionally, albumin.

3. A liquid pharmaceutical formulation according to claims 1, in which interferon-beta is recombinant.

5. A liquid pharmaceutical formulation according to claim 1, in which the buffer solution is acetate buffer.

6. A liquid pharmaceutical formulation according to claim 4, in which the buffer solution has a concentration of 0.01 M.

7. A liquid pharmaceutical formulation according to claim 1, which also comprises human albumin.

9. A process for the preparation of a pharmaceutical formulation according to claim 1, comprising combining interferon-beta with mannitol, a buffer at pH between 3.0 and 4.0 and, optionally albumin.

10. A container hermetically sealed in sterile conditions comprising the liquid pharmaceutical formulation according to claim 1 and appropriate for storage prior to use.